implantation (PCI) regarding CYP2C19 and ABCB1 genotypes.
Methods: A total number of 180 stable angina patients after an elective PCI were enrolled in the setting of a randomized, placebo-controlled clinical trial (NCT00638326). PR was measured 12-18 hours after a 600-mg loading dose of clopidogrel with light transmission aggregometry (LTA) using ADP 5 uM stimuli and with vasodilator-stimulated phosphorylation (VASP) assay. *2 and *3 single nucleotide polymorphisms (SNP) were amplified in case of CYP2C19 isoenzyme, while C3435T and G2677A/T SNP-s were tested in case of ABCB1 gene. The clinical endpoint of interest was the composite incidence of cardiovascular (CV) death, myocardial infarction (MI) or target vessel revascularization (TVR) at one year.
Results: Patients with *2 or *3 SNP-s had significantly higher PR compared to wild-type carriers by both LTA (*1*1: 26.7±14.5; *1*2/3: 31.7±13.4; *2*2: 45.2±11.8) and VASP (*1*1: 48.2±22.6; *1*2/3: 57.5±22.6; *2*2: 61.8±5.9) measurements. On the other hand, neither C3435T nor C2677A/T SNP affected PR. Homozygous subjects for two loss-of-function alleles of CYP2C19 isoenzyme had a 6.21-fold higher relative risk regarding the primary endpoint (HR: 6.21, 95%CI: 1.17-33.05, p<0.01), while patients heterozygous for a CYP2C19 SNP had similar outcome compared to wild-type carriers (HR: 0.90, 95%CI: 0.19-4.34, P=NS). We did not observe any difference in clinical outcomes regarding ABCB1 genotypes.
Conclusions: Among low-risk, stable angina patients after PCI, CYP2C19 *2 and *3 SNP-s significantly interfere with post-clopidogrel PR and clinical outcome. Although all carriers of the defective alleles had elevated PR, the excess ischemic risk was only present in poor metabolizer patients homozygous for two loss-of-function alleles. SNP-s in case of ABCB1 were not associated with PR or clinical outcome.

TCT-6

Net Adverse Clinical Events After Percutaneous Coronary Intervention in Patients Treated With Proton Pump Inhibitors In Conjunction With Clopidogrel

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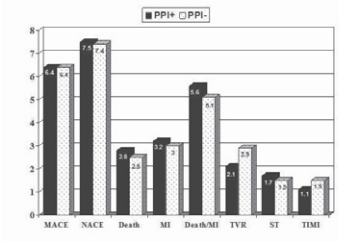
Objectives: We evaluated the impact of proton pump inhibitors (PPIs) on net adverse clinical events after percutaneous coronary intervention (PCI).
Methods: We studied 2651 consecutive patients who underwent uncomplicated coronary stenting for stable or unstable coronary disease (excluding cardiogenic shock) between '01-'07. Depending on the use of PPI at discharge, patients were divided into PPI (+) (n = 751) or PPI (-) (n = 1900) groups. All patients were prescribed aspirin indefinitely and a thienopyridine for 1-12 months. The study end-points were: time to occurrence of MACE, defined as composite of death, MI, TVR, stent thrombosis during the 6 months after PCI; and time to occurrence of net adverse clinical events [NACE, i.e. composite of MACE and TIMI (major or minor) bleeding]. Using propensity-adjusted Cox regression, we evaluated the independent effect of PPIs on study outcomes. Given the suspected stronger antagonism of clopidogrel by omeprazole and esomeprazole, subset analyses were performed comparing patients who received either of these 2 PPI agents (n = 312) with PPI (-) group.
Results: Significant baseline differences were seen PPI+ and PPI- patient groups. PPI+ and PPI- groups had similar rates of 6-month MACE (6.4 vs 6.4%) and NACE (7.5 vs 7.4%) (figure). In propensity-adjusted multivariate analyses, PPI use did not affect MACE, NACE, or any of the individual end-points. In subset analysis, the use of either omeprazole or esomeprazole was associated with lower rates of MACE (3.9 vs 6.4%, adjusted HR 0.51, p = 0.0256) and TVR (1.0 vs 3.0%, adjusted HR 0.32, CI 0.10-1.03, p = 0.056) compared to PPI- group.



Conclusions: The use of PPIs does not have any adverse influence on net adverse clinical events after PCI

TCT-7

Platelet Inhibition by Adjunctive Cilostazol Versus High Maintenance-Dose Clopidogrel in Patients With Acute Myocardial Infarction According to Cytochrome 2C19 Genotyping

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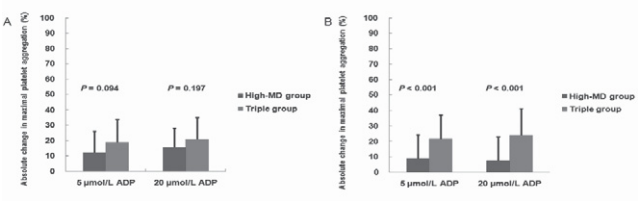
Objectives: The aim of this study was to assess the degree of platelet inhibition by adjunctive cilostazol in patients with acute myocardial infarction (AMI) according to *CYP2C19* genotyping.
Background: Although adjunctive cilostazol intensifies platelet inhibition in AMI patients, it is not established whether this regimen can overcome the loss-of-function effect of *CYP2C19* variant.
Methods: We randomly assigned 126 AMI patients with available *CYP2C19* genotyping to receive adjunctive cilostazol (triple group; n = 64) or high maintenance-dose (MD) clopidogrel of 150-mg/day (high-MD group; n = 62). Using conventional aggregometry and VerifyNow, platelet reactivity was measured at pre-discharge and 30-day follow-up. Primary endpoint was change in maximal platelet aggregation (Agg_{max}). High post-treatment platelet reactivity (HPPR) was defined as 5 μmol/l ADP-induced Agg_{max} > 50%.
Results: In non-carriers, the two groups did not differ with respect to changes of platelet measures, and could achieve fewer rates of HPPR at 30-day (< 5%). In carriers, changes of 5 and 20 μmol/l ADP-induced Agg_{max} were significantly higher in the triple (n = 39) versus high-MD group (n = 38) (21.8 ± 13.9% vs. 9.0 ± 13.3%, p < 0.001, and 24.2 ± 17.2% versus 7.7 ± 15.5%, p < 0.001, respectively). Likewise, changes in late platelet aggregation and $P2Y_{12}$ reaction unit were consistently greater in the triple vs. high-MD group. Fewer patients in the triple group met the criteria of HPPR at 30-day compared with the high-MD group (2.6% vs. 21.1%, p = 0.014).
Fig. absolute change of Agg_{max} in non-carriers (A) and carriers (B) of CYP2C19 variant.



Conclusions: Among AMI patients with *CYP2C19* variant, adjunctive cilostazol enhances platelet inhibition and reduces the rate of HPPR, as compared with high-MD clopidogrel. (ACCEL-AMI-*CYP2C19*; NCT00915733).

TCT-8

Does Gradual Tapering of Clopidogrel Ameliorate the Potential for Rebound Enhanced Platelet Aggregation post Sudden Discontinuation ?

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Background: Late stent thrombosis remains a major concern with drug eluting stents (DES). Retrospective analysis of such cases has shown a clustering of such events post sudden stoppage. Prior studies have shown a potential for enhanced platelet aggregation as a mechanism.
Aim: The aim of this work is to compare the platelet aggregation between sudden stopping (Group A) vs, gradual stopping of clopidogrel over a 2 week period(Group B) using the current gold standard Light Transmission Aggregometry (LTA)
Methods: A total of 136 patients were included in this study ; 74 patients (GP-A)who had sudden D/C of clopidogrel were compared to 62 patients(GP-B) who had gradual tapering over 2 weeks before complete cessation of clopidogrel ; this group were given clopidogrel for 3 days for 1 week then for only 2 days for 1 week before the clopidogrel was stopped. All patients had been on clopidogrel for at least 6 months with an adequate aggregatory response (>40% platelet inhibition) and had pre PCI LTA as well as 2 weeks post D/C clopidogrel RESULTS : The mean duration of clopidogrel therapy was 290 days (Gp-A) vs 329 (Gp-B)p<.01. The 2 groups were evenly matched except for more diabetics in Gp-A(39%vs29% , p<.05). LTA (5McM-ADP) pre clopidogrel was 67-91 with a mean of 76. Post D/C clopidogrel , the corresponding numbers were 78-121 with a mean of 93; (p<.05)in(GP-A)but were 68-94 with a mean of 77pre and 66-92 with a mean of 79 post gradual D/C (p=NS)(GP-B).Overall 12/74 patients in GP-A had a significant increase in platelet aggregation post sudden D/C vs. 0/62 in Gp-B (p<.01). Only 1 patient in GP-A had LST that occured 6 days post D/C clopidogrel.
Conclusion: LTA determined platelet aggregation revealed an enhanced rebound aggregation post sudden stopping of clopidogrel that was not shown after gradual tapering of clopidogrel over 2 weeks before complete stopping.

Bifurcation

150A

Wednesday, September 22, 2010, 3:30 pm – 5:30 pm

(Abstract Nos 9-16)

TCT-9

Impact of Bifurcation Angioplasty on Side Branch Ostium: Insights From BRANCH Trial

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Background: Restenosis of bifurcation lesions remains high even in the DES era due to post-procedural stent under-expansion, inadequate coverage, and/or multiple layers of overlapping stents at the side branch (SB) ostium and carina. The aim of this IVUS study was to investigate stent expansion and coverage at the SB ostium and carina in bifurcation lesions treated with the Medtronic Y-shaped bifurcation-dedicated stent (BDS; Medtronic CardioVascular, Santa Rosa, CA) and with the conventional side branch angioplasty (SBA).
Methods: Post procedure IVUS data of BDS (n=45) from the first-in-man, prospective, multicenter, non-randomized, single-arm BRANCH trial was compared with data of SBA (n=19) without provisional stent placement in the SB. IVUS analysis included 4 distinct locations: proximal main branch, bifurcation site, distal main branch, and SB. In addition to the standard 3D IVUS parameters, lumen symmetry at the border between the bifurcation site and each branch was calculated as minimum / maximum lumen diameters. Floating struts were defined as stent struts across the SB ostium.
Results: Lumen volume in SB was larger and a minimum lumen area <4 mm2 in SB was less frequent in BDS compared with SBA. The SB ostium was larger and more symmetric in BDS than in SBA. Floating struts at the SB ostium were detected less frequently in BDS (20.9 vs. 78.9%, p<0.0001), and the axial segment length with floating struts was significantly shorter in BDS compared with SBA (0.7 ± 0.4 vs. 1.5 ± 0.8 mm, p=0.019), suggesting better struts coverage at the carina in BDS than in SBA.